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Cote and doctoral student Wei Yao work on understanding one of the proteins that causes retinitis pigmentosa, a leading inherited cause of vision loss and blindness. Cote received a $1.1 million grant from the National Institutes of Health for this work. Credit: Lisa Nugent, UNH Photographic Services.

DURHAM, N.H. – Rick Cote, professor and chair of the department of molecular, cellular, and biomedical sciences at the University of New Hampshire, has received $1.1 million from the National Institutes of Health (NIH) for his ongoing research on one of the proteins that causes retinitis pigmentosa, a leading inherited cause of vision loss and blindness.

Retinitis pigmentosa, or RP, is a progressive disorder that affects 1.5 million people worldwide. People with RP typically experience a gradual decline in their vision in their youth, with symptoms most commonly including a loss of peripheral and night vision. By their forties, many people with RP are considered legally blind.

Cote and his UNH colleagues study the enzyme phosphodiesterase, or PDE, the central enzyme in the photoreceptor cells (rods and cones) that transform light into images. Cones affect color perception and discriminating visual work like reading, while rods control peripheral vision and vision in low light. But when PDE undergoes a genetic mutation, rods and cones can die, resulting in RP. Cote's work aims to better understand how PDE controls this photoreceptor signaling pathway, so that new therapies can be developed to treat RP to prevent vision loss.

"My research examines the fundamental mechanisms regulating the visual signaling pathway by the PDE enzyme," says Cote. "The knowledge we gain hopefully will be used in future clinical trials to slow or halt the progression of retinal diseases resulting from defects in this signaling pathway in rods and cones."

While this grant is the latest in more than two decades of continuous NIH support for Cote's research program, he admits "We're still pretty much in the dark about how defects in the PDE enzyme directly cause RP," he says. But constant advances in technology and in research methods used by his lab keep the work exciting and moving steadily forward.

Cote has not had to look far for some of the most innovative and sophisticated tools to advance his research. He's currently working with UNH's Hubbard Center for Genome Studies, led by Kelley Thomas, on a bioinformatics and evolutionary approach to understanding the structure and function of PDE. He's also tapped the pioneering analytical ultracentrifugation tools of UNH's Center to Advance Molecular Interaction Sciences (CAMIS), directed by Tom Laue.

"Tom came up with a new optical system that allowed us to see dynamic changes in the structure of PDE and the effects of mutations on its structure that we hadn't been able to approach in the past," says Cote.

Most recently, he has collaborated with Feixia Chu, assistant professor in the department of molecular, cellular and biomedical sciences, using an analytical technique called mass spectrometry to identify all of the proteins in the photoreceptor cell that bind to PDE. Cote describes this work as building a topographical map of the entire PDE signaling complex. "It's a wonderful tool for figuring out how PDE and other proteins assemble into a compact signaling complex that converts a light stimulus into a nerve impulse," he says.

Cote acknowledges that decades of fidelity to one research topic – while not unheard of – surprises even him. "When I started this work 20 years ago, I would have thought it would have had an end point," says Cote. "Instead, it's more like the petals of a flower. The more it opens, the more it reveals. Fortunately, the technological advances and new research tools are occurring at a rate that parallels the sophistication of the questions we want to answer."

Cote's research group includes senior scientists Karyn Cahill and Jun Zhang, research technician Sue Matte, doctoral students Wei Yao and Ken-Edwin Aryee, master's student Hannah Failing, as well as undergraduate

student researchers. In addition to the NIH, this work receives funding from the New Hampshire Agricultural Experiment Station.

The University of New Hampshire, founded in 1866, is a world-class public research university with the feel of a New England liberal arts college. A land, sea, and space-grant university, UNH is the state's flagship public institution, enrolling 12,200 undergraduate and 2,200 graduate students.

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Photograph available to download: http://unh.edu/news/cj_nr/2010/may/bp26cote.jpg
Caption: Cote and doctoral student Wei Yao work on understanding one of the proteins that causes retinitis pigmentosa, a leading inherited cause of vision loss and blindness. Cote received a $1.1 million grant from the National Institutes of Health for this work.
Credit: Lisa Nugent, UNH Photographic Services.

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